

AD-A184 483

ASYMMETRIES IN HEMISPHERIC CONTROL OF ATTENTION IN
SCHIZOPHRENIA(U) WASHINGTON UNIV ST LOUIS MO
M I POSNER ET AL 23 JUL 87 TR-87-8 N00014-86-K-0289

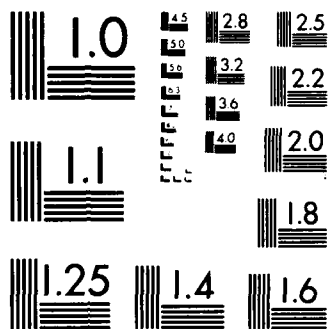
1/1

UNCLASSIFIED

F/G 5/8

NL





MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

AD-A184 483

ASYMMETRIES IN HEMISPHERIC CONTROL
OF ATTENTION IN SCHIZOPHRENIA

Michael I. Posner, Terrance S. Early, Eric M. Reiman,
Patricia J. Pardo and Meena Dhavan

Washington University, St. Louis and
McDonnell Center for Studies of Higher Brain Function

ONR 87-8

DTIC
ELECTE
SEP 11 1987
S D

Research sponsored by:

Personnel and Training Research Program,
Psychological Science Division,
Office of Naval Research

Under Control Number:

NO014-86-K-0289

Contract Authority Number:

NR-442a554

Reproduction in whole or part is permitted for any
purpose of the United States Government

DISTRIBUTION STATEMENT A
Approved for public release
Distribution Unlimited

A184 483

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION Unclassified			1b. RESTRICTIVE MARKINGS	
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release: distribution unlimited.	
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE				
4. PERFORMING ORGANIZATION REPORT NUMBER(S) Technical Report #87-8			5. MONITORING ORGANIZATION REPORT NUMBER(S)	
6a. NAME OF PERFORMING ORGANIZATION Washington University		6b. OFFICE SYMBOL (if applicable)		7a. NAME OF MONITORING ORGANIZATION Office of Naval Research (Code 1142PT) Personnel & Training Research Programs
6c. ADDRESS (City, State, and ZIP Code) 660 S. Euclid, Box 8111 Department of Neurology St. Louis, MO 63110			7b. ADDRESS (City, State, and ZIP Code) 800 North Quincy Street Arlington, VA 22217	
8a. NAME OF FUNDING / SPONSORING ORGANIZATION		8b. OFFICE SYMBOL (if applicable)		9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER N00014-86-KO289
8c. ADDRESS (City, State, and ZIP Code)			10. SOURCE OF FUNDING NUMBERS	
			PROGRAM ELEMENT NO. 61153N	TASK NO. RR04206
			WORK UNIT RR04206-OA	ACCESSION NO. NR442a554
11. TITLE (Include Security Classification) Asymmetries in Hemispheric Control of Attention in Schizophrenia				
12. PERSONAL AUTHOR(S) Michael I. Posner, Terrance S. Early, Eric M. Reiman, Patricia J. Pardo and Meena Dhawan				
13a. TYPE OF REPORT Technical		13b. TIME COVERED FROM 01MAY87 TO 01MAY88		14. DATE OF REPORT (Year, Month, Day) July 23, 1987
15. PAGE COUNT 28				
16. SUPPLEMENTARY NOTATION				
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)	
FIELD	GROUP	SUB-GROUP		
05	10			
19. ABSTRACT (Continue on reverse if necessary and identify by block number)				
20. DISTRIBUTION / AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input checked="" type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION Unclassified	
22a. NAME OF RESPONSIBLE INDIVIDUAL Michael I. Posner			22b. TELEPHONE (Include Area Code) (314) 362-3317	22c. OFFICE SYMBOL ONR 1142 PT

Asymmetries in Hemispheric Control of Attention in Schizophrenia

Michael I. Posner, Terrence S. Early,
Eric M. Reiman, Patricia J. Pardo and Meena Dhawan

McDonnell Center for Higher Brain Studies and
Departments of Neurology, Neurological Surgery, Psychiatry,
Psychology, Washington University, St. Louis

ABSTRACT

Investigators have long suggested that schizophrenia might be related to an impairment in the regulation of attention. In this report, we compare the performance of schizophrenic patients with normal control subjects in their ability to direct visual attention. In the first experiment, patients were distinguished from controls by a slower response to a target in the right visual field than to a target in the left visual field when attention was not first directed to the target location. In the second experiment, patients were distinguished from controls by a stronger bias in favor of symbolic information over language information about spatial direction. In both experiments, the patients demonstrated deficits in attention similar to patients from previous studies who had unilateral lesions of the left hemisphere.

The identification of performance abnormalities using tasks which are simple, have dissectable cognitive components, have been related to discrete neural systems, and control for non-specific variables provide the basis for constructing reasonable hypotheses about the cognitive psychology and functional neuroanatomy of schizophrenia.



Assigned For	
THIS GRA&I	<input checked="" type="checkbox"/>
DATE TAB	<input type="checkbox"/>
Classified	<input type="checkbox"/>
Classification	
by	
Date	
Exemption Codes	
Exemption Code	
Exemption Code	
A-1	

Schizophrenia has long been thought of as a disorder of attention (Matthysse, 1978). The concept of attention used by researchers has generally not been clearly tied either to specific cognitive operations or specific neural systems. Currently, the form of selective attention that has been examined in most detail is the ability to shift attention to areas of visual space to facilitate target detection. Cognitive studies have shown that cueing attention to a visual location, without movement of the eyes improves the efficiency of detecting targets as measured by reaction time (Posner, 1980), reduced threshold (Bashinski & Bachrach, 1980) and increased electrical activity from the cued location (Mangun, Hansen & Hillyard, 1986). These shifts of visual attention are closely time-locked to the presentation of the cue so that improvements in processing occur in the first 150 millisecon following the cue (Posner, 1980; Posner, et al, 1984). The covert shift of visual attention can also be divided into more specific mental operations of disengaging from the current focus of attention, moving attention to the cued location and engaging the target (Posner & Presti, 1987). Visual spatial attention can be viewed as a part of a larger attentional system involved in processing other forms of attention (Posner, Inhoff, Friedrich & Rafal, 1987).

Single cell studies with alert monkeys (Mountcastle, 1978; Wurtz, et al, 1980) and with brain injured patients (Posner, Walker, Friedrich & Rafal, 1984) suggest that a neural system involving the posterior parietal lobe and areas of the thalamus and midbrain form a system which controls such shifts of attention (Posner & Presti, 1987). Lesions of the parietal lobe appear to produce a deficit largely in the disengage operation, while midbrain lesions appear to disrupt the ability to move attention to the target (Posner & Presti, 1987).

These findings, based on patients with specific neurological lesions, can now be used to develop a more objective way to study disorders like schizophrenia that are supposed to involve attentional deficits but have an unknown organic basis. If specific deficits can be found in simple cognitive tasks such as the ability to shift attention, it might then be possible to determine the cognitive operations that are affected and use them to understand the neural systems involved in the disorder. This paper is a first step in that direction.

It has often been proposed that the deficit in schizophrenia predominantly involves the left hemisphere (Early, et al, 1986; Flor-Henry, 1983). If this is true and if the deficit involves visual spatial attention, one could predict that schizophrenics like left parietal patients, would show a relatively slow response to targets in the right visual field following cues to the left visual field. Experiment 1 examines this possibility.

Experiment 1

The first experiment compares patients with schizophrenia and normal volunteers in their ability to orient attention in response to peripheral visual cues. The hypothesis developed from the literature cited above is that schizophrenics will respond more slowly to unattended signals in the

right visual field than to those in the left visual field. When attention is cued to the location of the target the two fields should not differ. Since each visual field has direct projections to the contralateral hemisphere, this result would fit with a left hemisphere abnormality that interacts with attentional cues. Normals would be expected to show no asymmetries between visual fields.

Method

Subjects

Twelve subjects who satisfied DSM III-R criteria for schizophrenia, including a minimum duration of six months at either this time of study or the time of follow-up, were recruited through the psychiatry department at Washington University School of Medicine. Table 1 indicates their demographic characteristics, lifetime symptoms, duration of illness, and current medications.

The normals were recruited from ads in local newspapers. Both groups were paid \$5.00 per hour for their participation.

INSERT TABLE 1 ABOUT HERE

The age of the normals ranged from 19-44, there were 9 males and 21 females, 27 right-handers and 3 left-handers. The educational level of the normals in most cases involved at least a high school education with a small number having completed college.

Procedure

The procedure followed by schizophrenics and normals was identical and is shown schematically in Fig. 1.

INSERT Figure 1 ABOUT HERE

Subjects were seated in front of a cathode ray tube and instructed to maintain fixation on a central fixation cross. Approximately five degrees to the left or right of fixation (at 4 cm. distance) there was a 1° degree square. Within each block of 240 trials 20% were uncued. In these trials following intervals of 1100 or 1800 msec following the previous key press, the target (a bright star) occurred in the center of one of the two squares with equal probability. On cued trials, following a 1000 msec inter-trial interval, one of the two squares was brightened with equal probability and remained present until the subject responded. Thus, on cued trials there was either a 100 or 800 msec interval between the onset of the cue and the onset of the target. On 80% of the trials, the target, a bright star figure appeared in the middle of the brightened square and remained present until the subject responded. For the remaining 20% of the trials the target occurred in the opposite square from the one that had been

brightened and also remained present until the subject responded. The subject's task was to respond as rapidly as possible to the target by pressing a single key with the index finger of the dominant hand. We always waited three seconds for the response prior to terminating the trial and beginning the next trial. While the subjects were cautioned to remain with eyes fixed, there was no monitoring of eye movements in this study because previous work had shown that subjects were unlikely to move their eyes under these conditions where acuity was not necessary in order to make the response (Posner, Nissen & Ogden, 1977). Both schizophrenic and normal subjects were run through three identical blocks. There were four breaks within each block and substantial breaks between each block.

Results

The median reaction times in each condition for all blocks combined was calculated. In all cases the median response for each individual subject was taken as the basic data of the experiment. All reaction times less than 100 msec were considered as anticipations and were eliminated from the experiment. Reaction times beyond 3000 msec were also eliminated because of the characteristic of the program. These eliminated only a few reaction times from each subject.

The results of the experiment are shown in Figure 2.

INSERT FIGURE 2 ABOUT HERE

The data from the 12 schizophrenics were cast into an analysis of variance with cue condition (Valid, Invalid, No Cue), visual field of target (Left, Right), and interval as the major variables. There was a significant effect of cue, $F=18.3(2,22)$ $p<.001$; interval, $F=34.5(1,11)$ $p<.001$; and visual field, $F=9.8(1,11)$ $p<.009$. In addition, there was a significant cue by interval by field interaction, $F=8.3(2,22)$ $p<.002$. The data conformed very well to the hypothesis. There is clearly no significant difference between the visual fields in the valid condition and a very strong difference between visual fields in each of the other conditions, except the invalid at the 800 msec interval. Since the 100 millisecond cue to target interval is too short for any eye movements (Fischer & Ramsperger, 1984), it is the best interval for obtaining purely covert attention shifts.

In the invalid condition at the 100 msec interval, all 12 schizophrenics showed longer reaction times to the right visual field than to the left visual field, although in two cases this is quite small. The right minus left invalid reaction time differences at the 100 msec interval are shown for each schizophrenic subject in Table 1 (last column).

The averaged results of the normals shown in Fig. 2. Although all but one of the schizophrenics were male and the controls were heavily female, a preliminary examination of the gender effects in normals showed that the males and females did not differ. An ANOVA of the normal data showed a significant effect of cue condition $F(2,58) = 32.5$, $p < .01$, interval $F(1,29) = 101$, $p < .01$ and their interaction $F(2,58) = 9.3$, $p < .01$. These

reflect the usual advantage of valid over invalid reaction times and the general improvement of cued trials with interval following the cue which also serves as a warning interval.

Three of the schizophrenics had not previously been medicated while nine of them were receiving various forms of medication as shown in Table 1. The data from the three never-medicated and nine medicated subjects is shown in Figure 3. The never-medicated subjects showed

INSERT FIGURE 3 ABOUT HERE

longer reaction times but there is no hint of a difference in pattern between the two groups. Although this is not the most direct comparison, since one would like to test the same subjects before and following medication, it does suggest that deficits are not entirely a result of medication.

Although the average reaction time for normal subjects did not appear to differ as a function of visual field, there are some subjects who show considerable differences in their reaction times in the two visual fields. Figure 4 indicates the distribution of right - left reaction time differences at the 100 msec interval for schizophrenics and normals.

INSERT FIGURE 4 ABOUT HERE

The normal data appear to represent a normal distribution with a slightly negative mean. The advantage of the right visual field in the normal data may reflect the use of the dominant (right hand) by most normals since the right targets would be processed initially by the left hemisphere that also controls the responding hand. Only one of the 30 normals has a reaction time difference above the mean for the schizophrenic subjects.

A subset of 17 of the 30 normals were retested a week later. We found high test retest reliabilities for the valid trials (.9), somewhat lower reliabilities for the invalid trials (.75) and the no cue trials were much less reliable (.55). The right - left visual field differences at 100 millisecond showed a test retest reliability of .41 suggesting that there was a somewhat stable tendency of some normals to show a visual field deficit similar to schizophrenics.

Conclusions

The results of Experiment 1 show quite clearly that schizophrenic patients have slower reaction times to right visual field targets than to left visual field targets when their attention is not first focused on the location of the target. This appears to be most clear under conditions where attention is first diverted to the left visual field and there is only a short time between cue and target (the 100 msec interval). This is also the condition where eye movements are least likely so that it

represents the best data for making the comparison. These disadvantages for the right visual field are not present in most normal subjects.

The abnormalities identified here in the schizophrenic patients have a strong resemblance to those found in patients with left parietal lesions (Posner, et al, 1984). Our interpretation has been that the parietal deficit is related to an inability to disengage from an ipsilesional cue in order to shift attention to a contralesional target. If schizophrenics had deficits in the left parietal lobe one would expect difficulty in directing attention to the right visual field targets when attention had been cued to the left visual field. However, there is another aspect of the data that appears different. The schizophrenics show little evidence for an attention shift to targets that occur in the left visual field. The advantage of valid over invalid trials for left visual field targets shown as solid lines in Figure 1 are much smaller than for normals. This finding leads to our hesitancy in identifying the pattern found in Experiment 1 with the left parietal deficit.

An inspection of Table 1 suggests the possibility that patients with auditory hallucinations manifest this effect most clearly. While we did not score the auditory hallucinations during the experiment itself, several of the patients were observed to be talking aloud during the experiment. Moreover, Bick & Kinsbourne (1987), recently reported that auditory hallucinations among schizophrenics can be reduced by requiring them to move their mouths. Their data suggest that the voices heard by the schizophrenics may in fact be coming from their own vocalizations, but they have lost the tag that indicates that they are self initiated. In order to determine whether language processing by itself could lead to the schizophrenic pattern, it seemed reasonable to see if normals would show the right visual field disadvantage found in schizophrenics if they were involved in a language task at the same time. Experiment 2 was designed to explore this possibility.

Experiment 2

In this experiment spatial orienting involved one block of trials of the same spatial orienting task as we have described previously. In two other blocks of trials in addition to the primary task, subjects also "shadowed" a story aloud as described below. The hypothesis was that during shadowing these normal subjects would show a pattern of performance that resembled the schizophrenic subjects.

Method

Subjects

Twenty normal subjects recruited before (two left-handed and 18 right-handed) were tested for three blocks of orienting. Seventeen of the subjects had participated in Experiment 1.

Stimuli

The tests were the same as in Experiment 1 with the addition of an auditory tape containing a reading by Gore Vidal of his novel Abraham Lincoln.

Procedure

Three blocks of orienting tasks were performed by each subject. The shadowing task was used in the first and third blocks. The shadowing task involved repetition of the auditory tape with the subject instructed to use a minimal lag between the tape and his oral reproduction. The subject was given practice in shadowing until he felt comfortable with the task. The subjects were instructed to perform the tasks while pressing a key on appearance of the star in any one of the squares while continuing to shadow.

Results

The results for the 100 msec condition for the spatial task performed by itself is shown in Fig. 5. The reaction times are very similar to those found in this condition in Experiment 1. The mean reaction time at the 100 msec condition in the divided attention condition is shown in the upper two lines of Fig. 4. Two features of these data are of interest.

INSERT FIG. 5 ABOUT HERE

Note that left visual field stimuli during shadowing give a relatively flat reaction time function between the valid and invalid conditions just as is found for the schizophrenic subjects in Experiment 1. Moreover, the advantage of the left visual field over the right visual field is larger in the divided attention condition than in any other of the conditions of the experiment.

An overall ANOVA of the data of the experiment revealed a main effect of attention condition (focus vs divided) $F(1/19) = 40.8$, $p < .01$; Cue (valid, invalid, no cue) $F(2/38) = 30.6$, $p < .01$; interval $F(1/19) = 102.9$, $p < .01$ and the interaction of cue and interval $F(2/38) = 3.7$, $p < .05$. However, there was no overall main effect of visual field nor any interactions of visual field with cueing. Thus there was no statistical support in the overall analysis for the right visual field disadvantage while shadowing. To explore this further we broke down the shadowing data into the two individual blocks and subjected the valid and invalid trials at 100 msec to a second analysis. These were the conditions that revealed the schizophrenic pattern in Experiment 1. In addition to a significant effect of cue $F(1/19) = 5.9$, $p < .02$; there is now a significant effect of cue by field reflecting the longer reaction times in the right visual field on invalid trials $F(1/19) = 4.4$, $p < .05$.

We further broke down the data by dividing the subjects who were faster than average and slower than average on no cue trials occurring 1100 msec

after the previous response. The slow subjects showed a much larger difference between visual fields while shadowing (33 msec) than did the fast subjects (8 msec). While this is still a smaller effect than found for the schizophrenic subjects, it does suggest that slower overall performance in the visual task does leave the person open to greater interference from the language processing.

Normals while shadowing seem to show a tendency for the same pattern as do schizophrenics. The overall reaction times of normals while shadowing were similar to those found for schizophrenics (Fig. 1). However, even with twice as many subjects as used in Experiment 1 and even with a very powerful divided attention language task (shadowing) that produces a 100 msec increase in reaction time, we found much weaker effects for normals than were found in Experiment 1 for schizophrenics.

Conclusions

Experiment 2 suggests that at least some of the effects of attention found in the schizophrenics can be mimicked in normals during shadowing. However, there seems to be a much weaker effect in normals than we have found in either the medicated or non-medicated schizophrenics. We conclude that although there may be some involvement of auditory hallucinations in the creation of the effects, they cannot be clearly attributed to the auditory hallucinations by themselves. Clearly the shadowing task occupied the left hemisphere language system quite strongly and in this sense was probably more demanding than whatever auditory hallucinations occurred to the schizophrenics during the experiment. Of course shadowing is not a duplicate for the emotional experiences involved in hallucinations. We tentatively conclude that the results found in schizophrenics are not solely due to the divided attention produced by dealing with language at the same time as dealing with the visual spatial attention, but this is likely an aspect of the problem. In either case, these results implicate language functioning in the spatial deficit to some degree.

Experiment 3: Spatial and Language Conflict

Experiment 2 provided some support for the view that the effect of schizophrenia on spatial orienting in the right visual field might be due to an interaction between auditory language and spatial orienting.

The present experiment looks directly at a task in which conflict is introduced between a spatial and a linguistic cue. In this task the subject receives either an arrow that points to the left or right or the visual word left or right. In "arrow blocks" the response is to be made by pressing a left or right key in the direction of the arrow, while in the "word blocks" the subject presses the key corresponding to the word. The conditions are shown in Figure 6. In previous work with stroke patients (Walker, et al, 1983; Sandson & Posner, 1987), we found that patients with right hemisphere lesions are dominated by the word, while patients with left hemisphere lesions are dominated by the arrow. In a recent study of closed head injury patients, we showed that dominance in the arrow-word conflict test agreed with the visual field that showed slowing in invalid trials in the covert orienting task (Walker, Friedrich & Posner, 1983).

These findings would suggest that schizophrenic patients would be faster in responding to the arrow stimulus and receive more interference from the arrow on the word response than the reverse.

To study this we employed twelve normals and ten schizophrenics in the arrow-word experiment.

Method

Subjects: Ten of the fourteen schizophrenics listed in Table 1 were run in this experiment. It was run at the same time as Experiment 1. Six of the patients were medicated at the time they were run, while four had never received antipsychotic medication. Twelve normals recruited in the same way as Experiments 1 and 2 were also run in this study.

Procedure: In this study, schizophrenic patients performed four blocks of 96 trials. In two of the blocks they were instructed to respond to the arrow and in two blocks they were instructed to respond to the word. Within each block 32 trials had the instructed stimulus alone, 32 trials had the instructed and non-instructed stimulus together and in agreement, and 32 had the two in conflict. For normals one block of attend word and one block of attend arrow of 192 trials each were run in counterbalanced order. Each trial began with a central fixation cross, followed .5 sec later by the stimulus. On half the trials the instructed stimulus was above the fixation and uninstructed one below fixation and the other half were reversed. The subjects rested the index and middle fingers of the dominant hand on a key board and were instructed to press the key in the direction indicated by the instructed stimulus.

Results

The mean of the mean reaction times for the ten schizophrenic and twelve normal subjects are shown in Figure 7.

INSERT FIGURE 7 ABOUT HERE

A statistical analysis of the data showed a main effect of group (normal vs. schiz.) $F(1/20) = 8.3$, $p < .01$, condition (alone, compatible, incompatible) $F(2/40) = 15.6$, $p < .01$ and attend instruction (arrow vs. word) X condition $F(2/40) = 5.3$, $p < .01$. The normal data also showed strong effects of condition but no significant main effect of attention instruction or interaction between attention instruction and condition. The schizophrenic data showed a significant interaction between attend instruction and condition $F(2/18) = 3.9$, $p < .05$. The interaction reflects the particularly long reaction times found in the word instruction when the word conflicts with the arrow. This tendency is also confirmed in the percentage correct responses (see parentheses in Figure 7). This condition shows 10% more errors than any of the other conditions of the experiment.

The findings shown in Figure 7 for schizophrenics mask an even more powerful results when the data are broken down between the four never medicated patients and the six patients on medication. As can be seen in Figure 8, the never medicated schizophrenics have much slower reaction times and high error rates in the attend word condition than in the attend arrow condition. Despite the very small numbers in this between group comparison, the interaction of medication with attend instruction (arrow vs. word) is significant $F(1,8) = 5.4, p < .05$. It appears that the medication worsens performance on the arrow and improves it on the word condition so that the six medicated patients like normals (see Fig. 6) show little difference in reaction time between the two instruction conditions.

INSERT FIG. 8 ABOUT HERE

A more direct test of the effect of medication on conflict is to compare the same subjects before and after medication. We have so far obtained data on four subjects run before ever being medicated and following medication. Three of the subjects are the same as those shown in Fig. 8 and one is a new subject (RS) (See Table 1). The results are shown in Fig. 9. Once again, these preliminary data suggest an improvement in the attend word condition particularly when it conflicts with the arrow. However, for these subjects the attend arrow condition does not show any dramatic worsening of performance.

INSERT FIG. 9 ABOUT HERE

The pre/post- medication comparison involves only a total of four subjects. Moreover, the comparison can reflect practice as well as medication effects. The comparison shown in Fig. 8 is free of practice effects, but of course is a between subjects comparison. By combining the two results, it seems safe to conclude that medication improves processing of the word in comparison to the arrow. The schizophrenics prior to medication seem to have a relative deficit in left hemisphere processing that is partly related to their tendency to activate the left hemisphere with hallucinatory language information, but which cannot be completely accounted for by that effect.

DISCUSSION

A specific left hemispheric abnormality in schizophrenia is strongly suggested by studies using methods as diverse as neuropsychological testing, dichotic listening, tachistoscopic visual hemifield testing, power spectrum EEG, evoked potentials to auditory, visual and somatosensory stimuli, CT, PET, and neuropathological studies. These studies have been the subject of a number of excellent recent reviews (Gruzelier, 1985; Seidman, 1983). The results presented here extend the evidence for lateralized dysfunction in schizophrenia by demonstrating left hemispheric problems in directed attention in patients with schizophrenia.

While it has been widely accepted that schizophrenia involves a disorder of attention there has been little agreement on what is meant by the term and what the anatomical implication of an attentional disorder might be. The first step in overcoming this problem is to define simple experimental tests that measure attention abnormalities.

The covert attention task used in our first experiment allows one to examine the efficiency of processing target events when attention has either been drawn to their location or to a different location. The finding that schizophrenics are slow in processing right visual field targets when attention is not correctly cued to the target provides evidence of a deficit that cannot be reasonably be ascribed to motivation, failure to understand instructions of other general factors. A reduced efficiency in processing right visual field targets that interacts with cues suggests an asymmetric attentional disorder.

In previous work the orienting of visual attention has been described in terms of three more elementary mental operations (Posner & Presti, 1987). The person must first disengage attention from the current focus, move attention to a new location and then engage the target at the new location. Deficits in these operations have been associated with parietal, midbrain and thalamic lesions respectively. The poor performance shown by schizophrenic patients for invalid targets in the right visual field resembles what we found in patients with left parietal lesions. However, in contrast to the deficits found in the patients with left parietal lesions, the deficits in the schizophrenics are much smaller, appear only at the shortest cue to target intervals, and are accompanied by a smaller than normal difference between invalid and valid reaction times in the left visual field.

Previous work suggested that attention to language and visual spatial attention interact (Posner, et al, 1987). Our second experiment indicates that language processing can create in normals a pattern of interference not unlike that found in schizophrenics, although not as strong. This fact suggests that the source of the schizophrenic deficit might lie in the anterior systems that coordinate attention to visual location and language. Our third experiment provides some support for this interpretation by showing that schizophrenic patients are slow in processing visual words in comparison to symbolic directional cues, particularly prior to medication. This deficit has also been found in neurological patients with left hemisphere lesions and in closed head injury patients with predominantly left hemisphere lesions.

The current results provide only a short step toward a combined anatomical-cognitive description of the deficit found in schizophrenic patients. One interpretation of them suggests that there is basic left posterior (parietal) deficit that produces the spatial attention findings found in Experiment 1. This deficit, which is not affected by medication, would be separate and in a sense more fundamental than deficits in language which are greatly affected by medication. A different view argues that the deficit involves a neural system that controls attention both to visual space and to language processing. It is of great interest that recent

results have suggested circuits that involve posterior parietal areas and dorsolateral prefrontal cortex that pass through the globus pallidus (Alexander, Delong & Strick, 1986). In a recent study employing positron emission tomography (PET), we found that never medicated schizophrenics had an abnormality in the left globus pallidus (Early, Reiman, Raichle & Spitznagel, 1986). PET studies on normal subjects involved in processing visual and auditory words, also performed at our institution, have implicated the left dorsolateral prefrontal cortex in retrieval of word associations (Petersen, et al, 1986; Petersen, et al, 1987). In unpublished work, we found that two patients with basal ganglia lesions showed spatial orienting deficits in the visual field opposite the lesion similar to those found in the right visual field of schizophrenics. It is possible that deficits in these frontal-basal ganglia-parietal pathways may provide the basis for spatial orienting and language abnormalities that we report in schizophrenic patients.

In this study, we employed simple tasks which have several important features. First, they have dissectable cognitive components. Second, they are thought to involve discrete neural systems. Finally, they utilize a within-subject control in an effort to minimize the effects of non-specific variables such as arousal, effort, motivation, and frustration.

Cognitive tasks such as these can now be employed to investigate the functional neuroanatomy of schizophrenia. In our laboratory, PET can be used to make multiple 40-second measurements of regional cerebral blood flow (CBF) in the same subject (Petersen, et al, 1986; Petersen, et al, 1987). Since CBF reflects local neuronal activity (Fox & Raichle, 1986), subjects can be studied during tasks of systematically higher complexity in order to relate dissectable cognitive operations to discrete neural systems.

Reasonable goals for cognitive research in schizophrenia include the identification of the fundamental cognitive operations and the corresponding neural systems which are dysfunctional. Tasks which permit the isolation of elementary operations, like those described in this study, are an important part of this strategy.

References

1. Matthyse, S. Missing Links. In Wynne, et al., (eds) Nature of schizophrenia. New York:Wiley, 1978.
2. Posner, M.I. Orienting of attention. The 7th Sir F. C. Bartlett Lecture. Quarterly Journal of Experimental Psychology, 1980, 32:3-25.
3. Bashinski, H.S. & Bachrach, V.R. Enhancement of perceptual sensitivity as the result of selectively attending to spatial locations. Perception and Psychophysics, 1980, 28:241-248.
4. Mangun, G.R., Hansen, J.C. & Hillyard, S.A. The spatial orienting of attention: sensory facilitation or response bias? 1986 ONR Technical Report SDEPL 001.
5. Posner, M.I., Walker, J.A., Friedrich, F.J. and Rafal, R.D. Effects of parietal lobe injury on covert orienting of visual attention. J. of Neurosci. 1984, 4, 1863-1874.
6. Posner, M.I. & Presti, D. Selective attention and cognitive control. Trends in Neuroscience, 1987, 10:12-17.
7. Posner, M.I., Inhoff, A., Friedrich, F.J. & Rafal, R.D. (1987) Isolating attentional systems: A cognitive-anatomical analysis. Psychobiology, 15, (2), 107-121.
8. Mountcastle, V. Brain systems for directed attention. J. Royal Soc. of Med. 1978, 71, 14-27.
9. Wurtz, R.H., Goldberg, E. and Robinson, D.L. Behavioral modulation of visual responses in the monkey: stimulus selection for attention and movement. In Progress in Psych. Biol. and Physiol. Psych. 9, 1980, 43-83.
10. Early, T.S., Reiman, E.M., Raichle, M.E. and Spitznagel, E.L. Left globus pallidus abnormality in never-medicated patients with schizophrenia. Proc. Nat. Acad. of Sci. 1986, 84:561-562.
11. Flor-Henry P. Hemisyndromes of temporal lobe epilepsy. In Myslobodsky, M.S. ed. Hemisyndromes New York: Academic, 1983.
12. Posner, M.I., Nissen, M.J., & Ogden, W.C. Attended and unattended processing modes: The role of set for spatial location. In H.J. Pick (Ed.), Modes of Perception. Hillsdale, N.J.:Lawrence Erlbaum Associates, 1977.
13. Fischer, B. & Ramsperger. Human express saccades: extremely short reaction times of goal directed eye movements. Exp. Brain Res. (1984) 57:191-195.

14. Bick & Kinsbourne, Auditory hallucinations and subvocal speech in schizophrenic subjects. *Am. J. of Psychiatry*, 1987, 144:222-225.
15. Walker, J.A., Friedrich, F.J., & Posner, M.I. Spatial conflict in parietal lesions. Paper presented to International Neuropsychology Society, 1983, San Diego.
16. Sandson, J. and Posner, M.I. Attention imbalances following head injury. Williams, J.M. (ed) *Cognitive Foundations of Neuropsychology*, Plena, In Press.
17. Gruzelier, J. Schizophrenia: Central nervous systems signs of schizophrenia. In *Handbook of Clinical Neurology* (46), *Neurobehavioral Disorders*, Chapter 29, 486-521. A.M. Fredericks (Ed.) Elsevier Publ. 1985.
18. Seidman, L.J. Schizophrenia and brain dysfunction: An integration of recent diagnostic findings. *Psychological Bulletin*, 1983, Volume 94, Number 2, 195-238.
19. Alexander, G.E., DeLong, M.R., and Strick, P.L. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Ann. R. Neurosci.* 1986, 9, 357-381.
20. Petersen, S.E., Fox, P.T., Posner, M.I., Mintun, M.A. & Raichle, M.E. Focal brain activity during visual language tasks as measured with averaged PET images of evoked CBF change. *Soc. Neurosci. Abstr.*, 1986, 12:1161.
21. Petersen, S.E., Fox, P.T., Posner, M.I. & Raichle, M.E. A comparison of auditory and visual processing of single words using averaged images of cerebral blood flow change. *Soc. Neurosci. Abstr.*, 1987.
22. Fox, P.T. & Raichle, M.E. Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in man. *Proc. Natl. Acad. Sci.* 1986, 83:1140-144.

FIGURE CAPTIONS

Figure 1. Schematic diagram of the covert visual orienting task. The cue involves brightening of one of the peripheral boxes. When the target (a star) appears on the cued side the condition is valid and when it appears on the uncued side it is called invalid (see text).

Figure 2. Mean of mean reaction times for twelve diagnosed schizophrenics and thirty normal subjects in spatial orienting task as a function of cued condition [null (no cue), valid, invalid], cue to target interval (100, 800) and visual field (left, right).

Figure 3. Mean of mean reaction time for three never medicated schizophrenics and nine different medicated schizophrenics in spatial orienting task as a function of cue condition and visual field for 100 msec cue to target interval.

Figure 4. Distribution of advantage right - left visual field reaction times (RT) in spatial orienting for twelve schizophrenic and 30 normal subjects in the invalid condition at the 100 msec interval.

Figure 5. Mean of mean reaction times for 20 normal subjects when doing the spatial orienting task alone (focus) and together with auditory shadowing (divided).

Figure 6. Schematic diagram of the arrow-word conflict task.

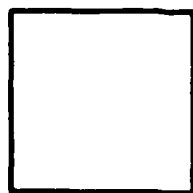
Figure 7. Mean of the mean reaction times for ten schizophrenic and twelve normal subjects in arrow-word conflict task as a function of stimulus condition (alone, compatible, incompatible) and instruction condition (attend arrow, attend word) mean % correct is shown in parentheses.

Figure 8. Mean of the mean reaction times in arrow-word conflict task for four never-medicated schizophrenics and a group of six different schizophrenics on medication mean % correct is shown in parentheses.

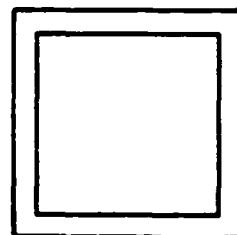
Figure 9. Mean reaction time in the arrow-word conflict task for four patients prior to medication (solid) and the same four patients following medication (dashed). Mean % correct is shown in parentheses.

Fig. 1

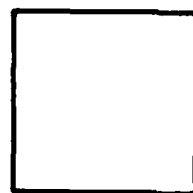
VALID
TRIAL



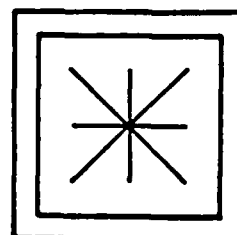
+



CUE

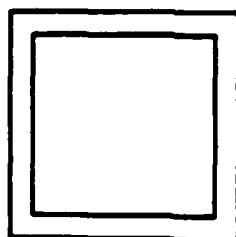


+



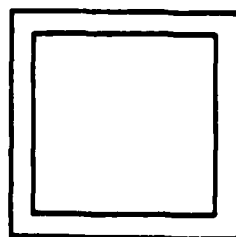
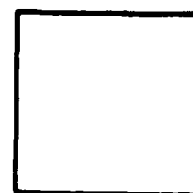
TARGET

INVALID
TRIAL

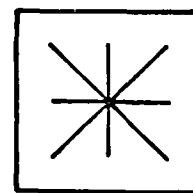


CUE

+



+



TARGET

Fig. 2

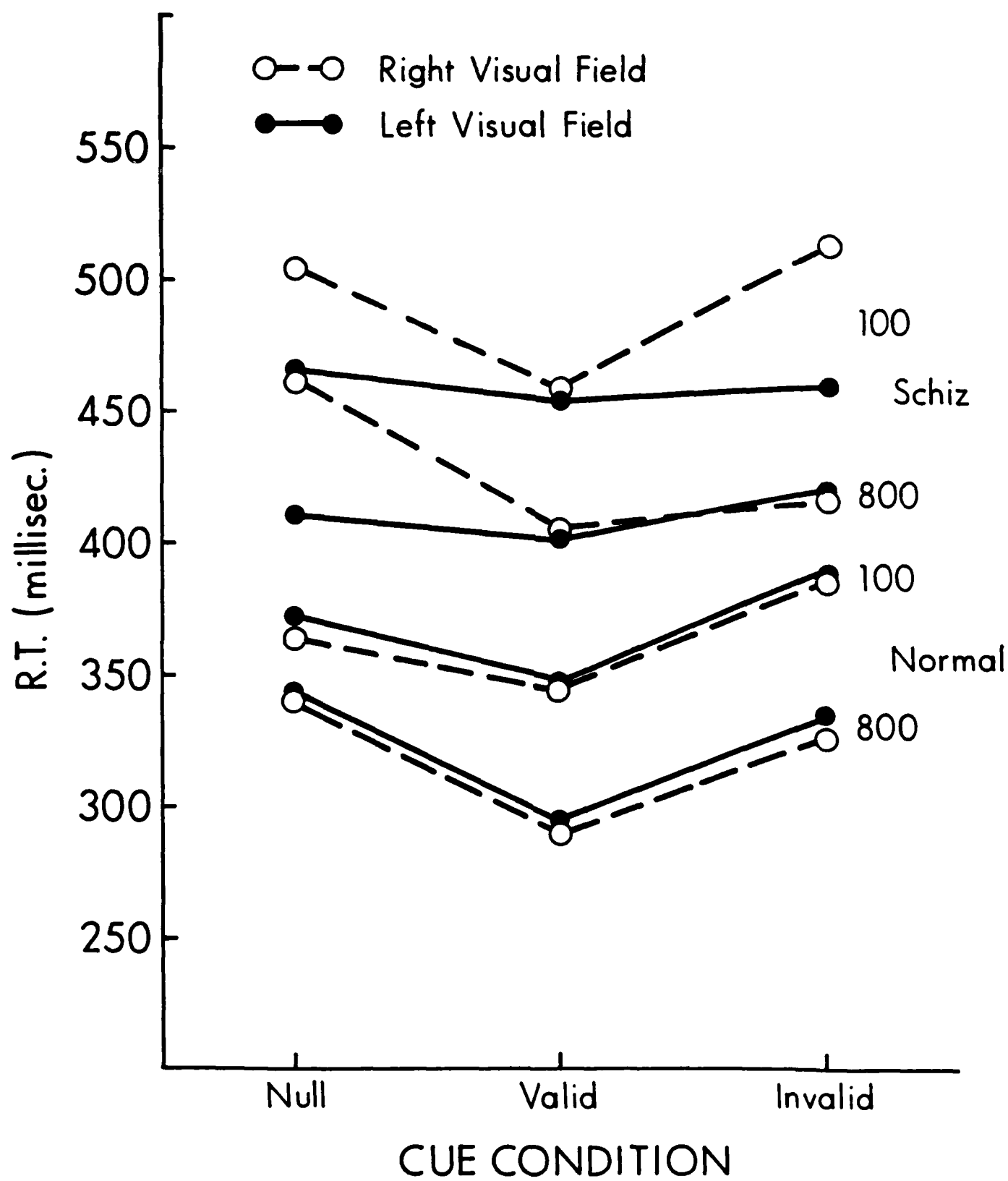


Fig. 3

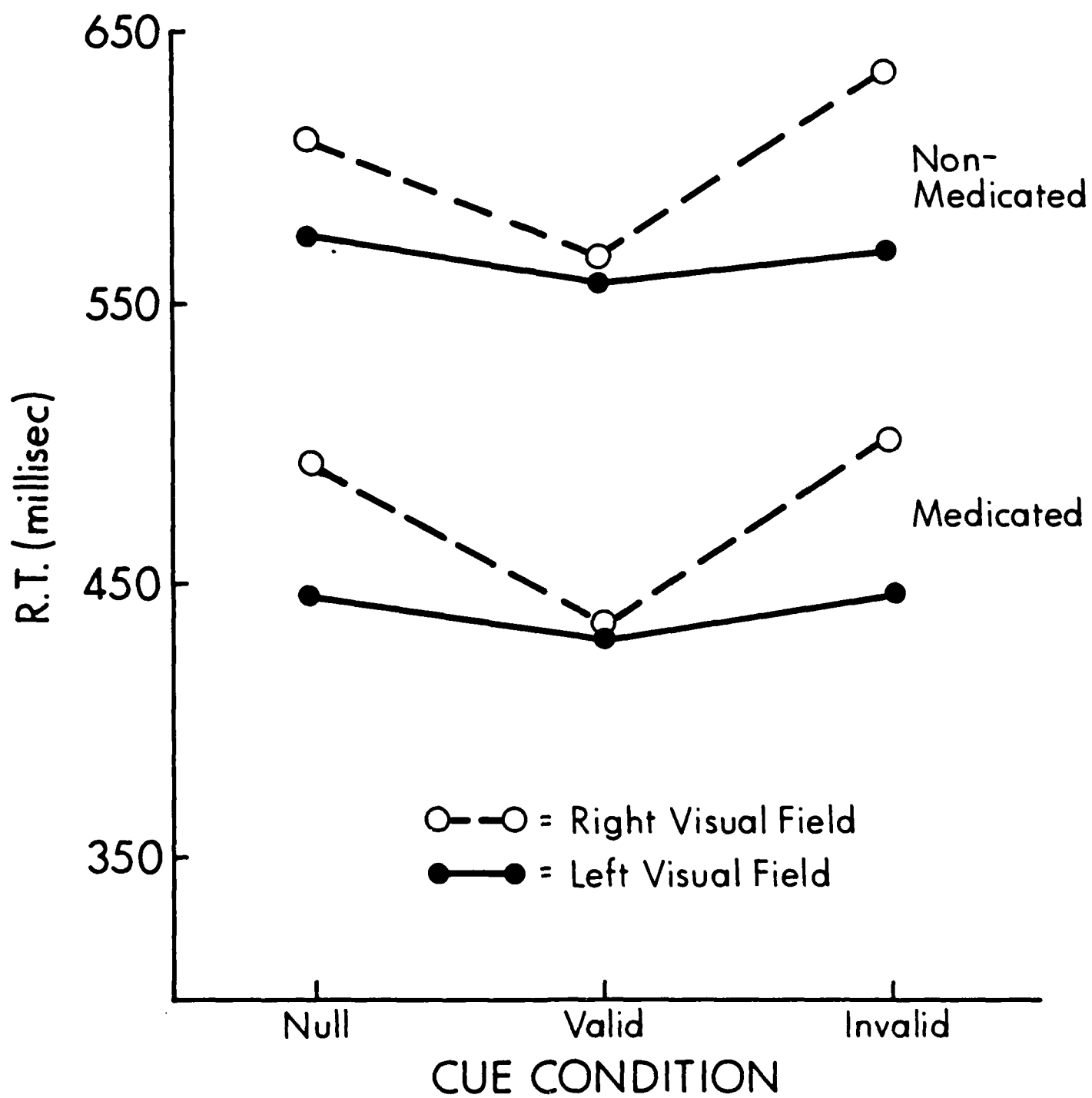


Fig. 4

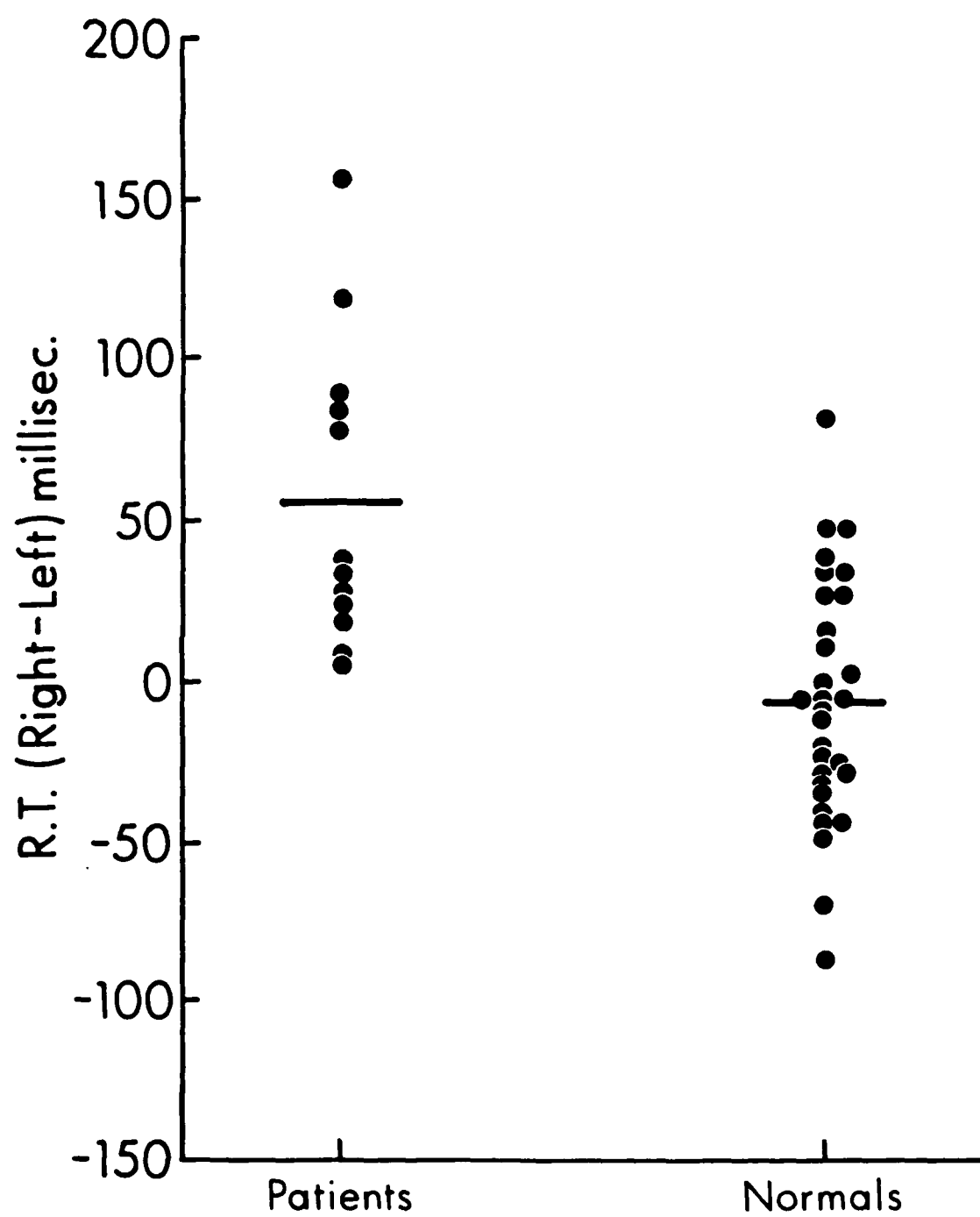


Fig. 5

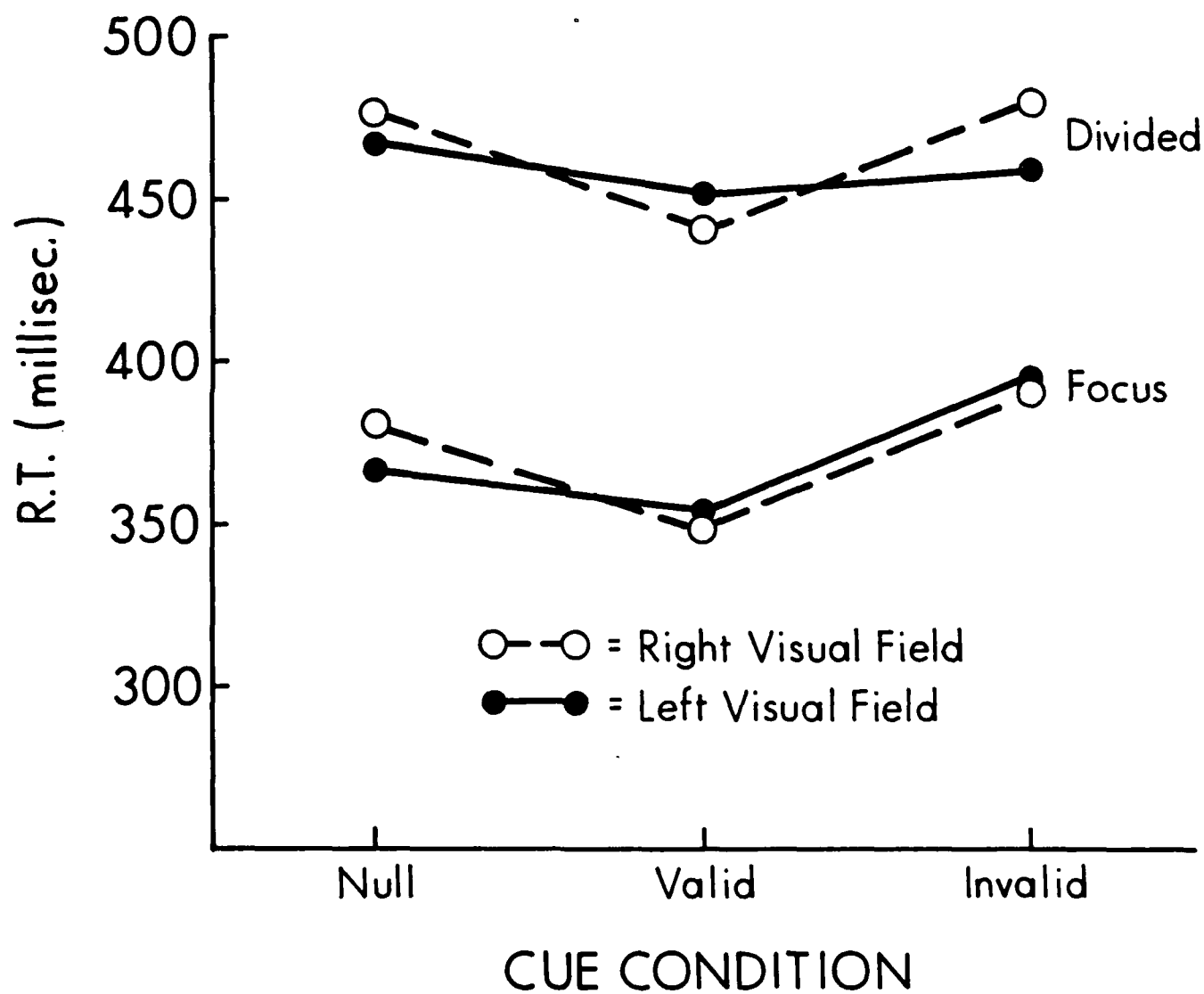


Fig. 6

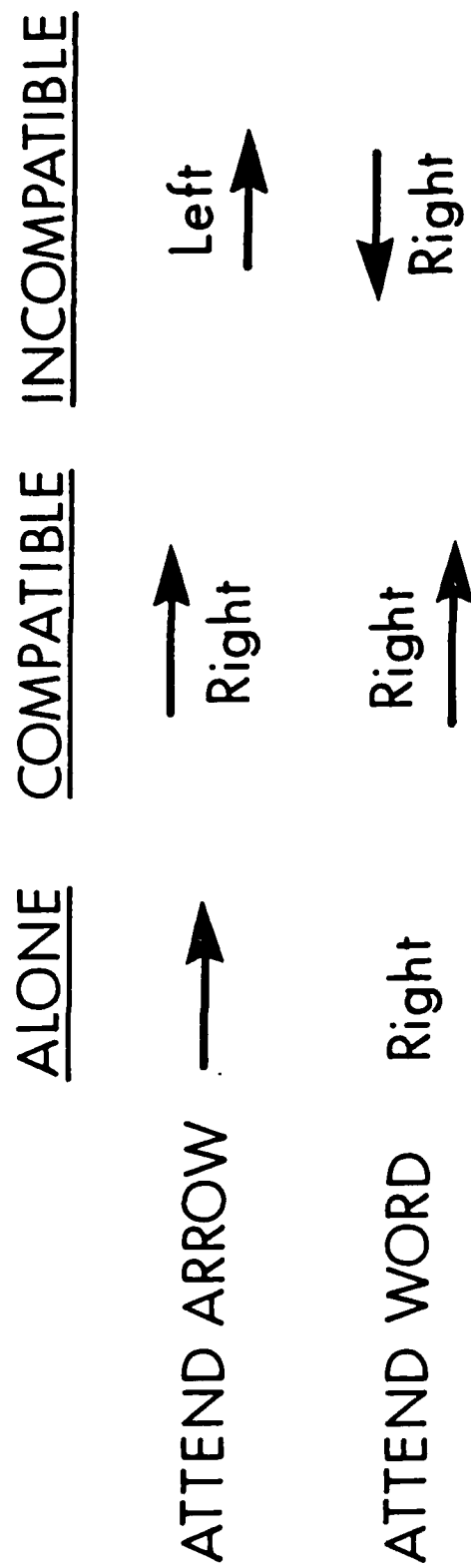


Fig. 7

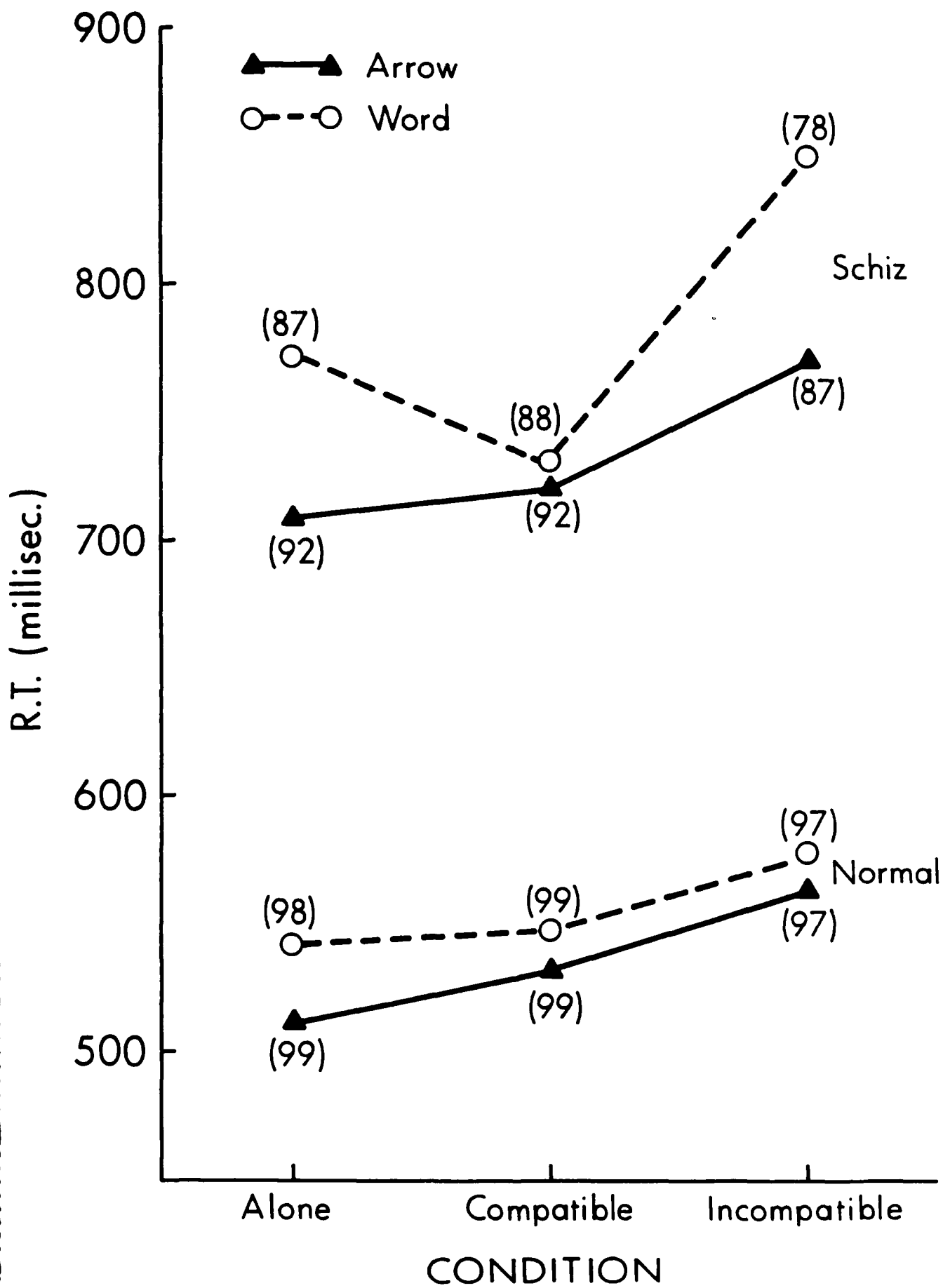
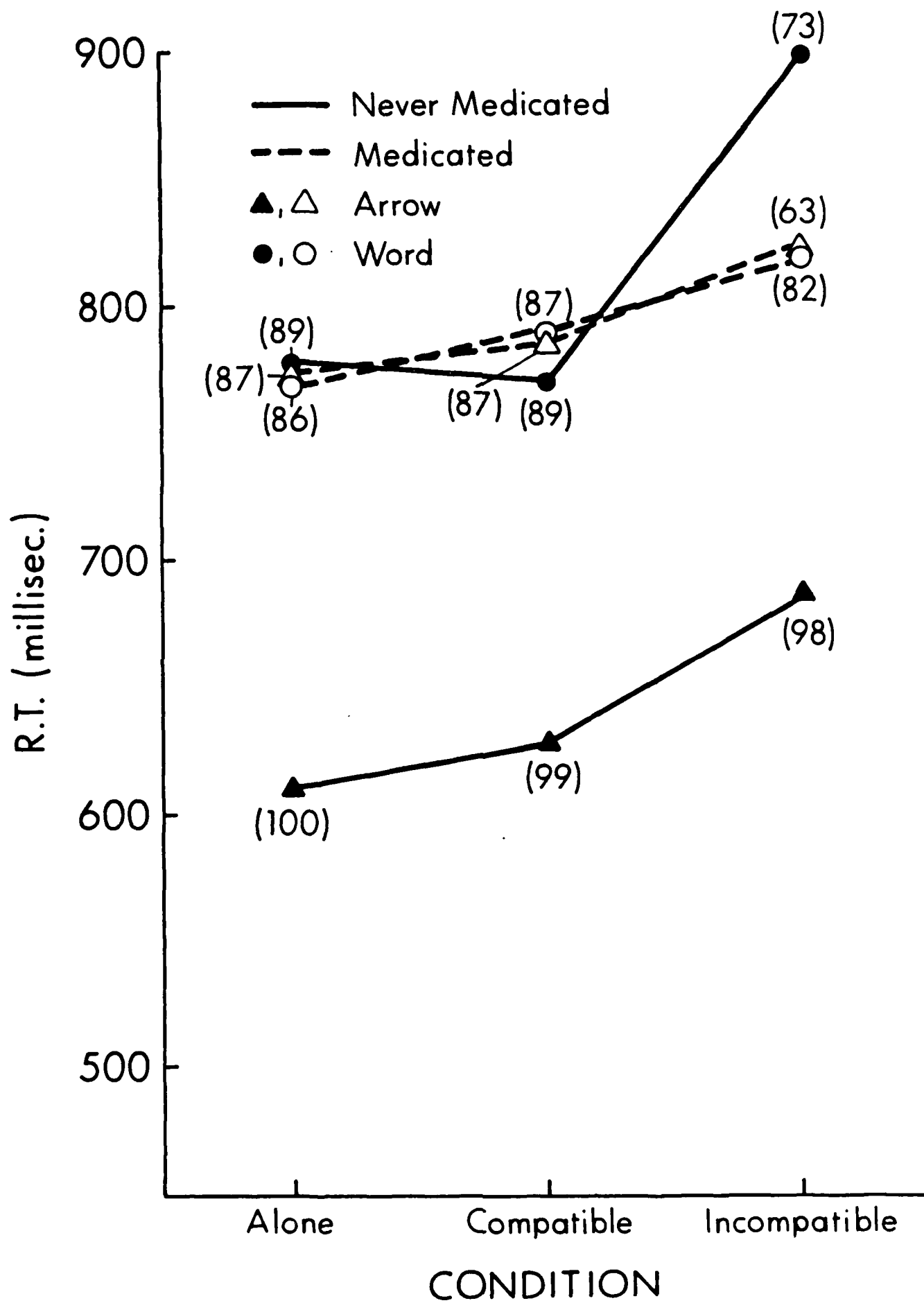


Fig. 8



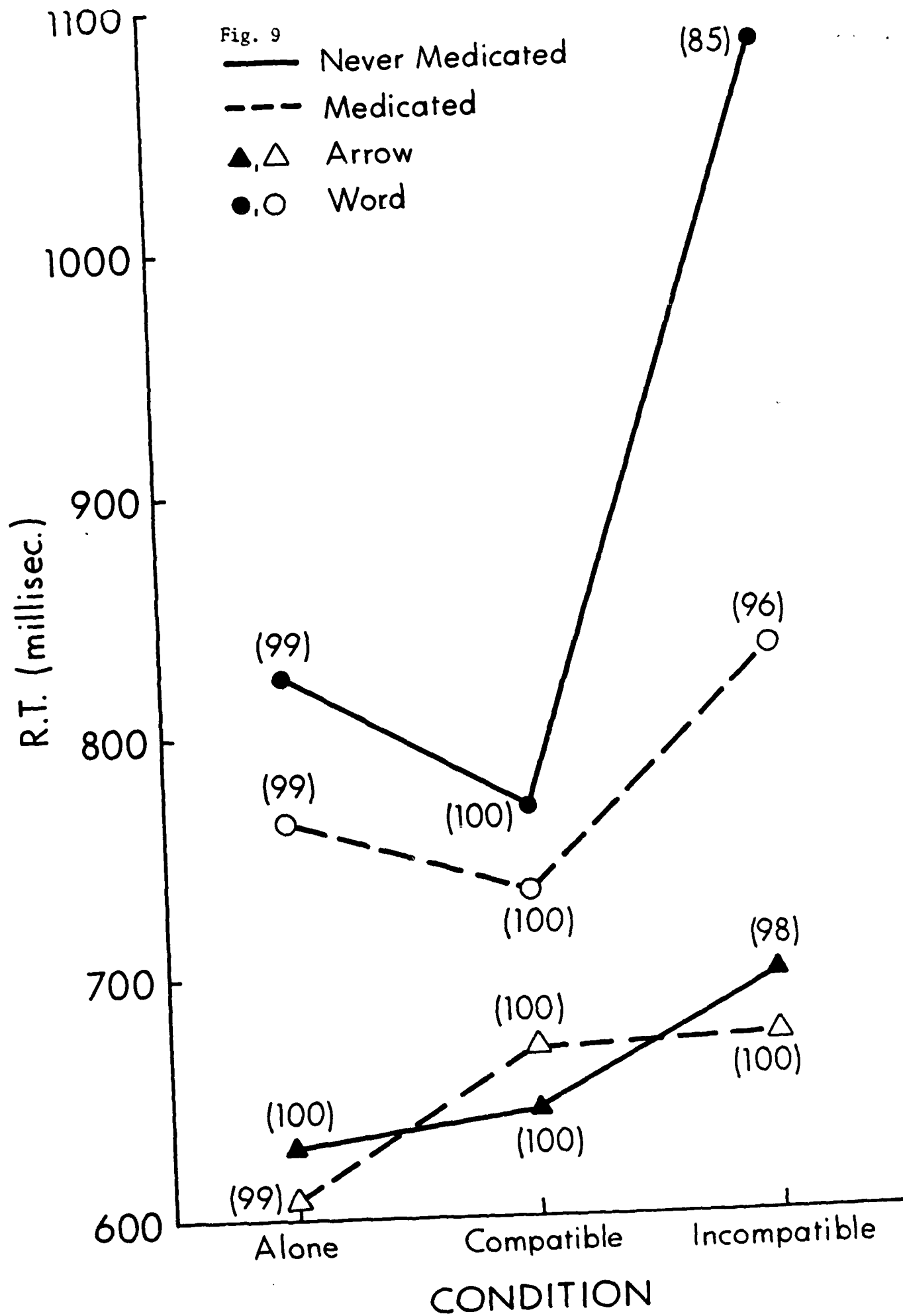


Table 1
Characteristics of Schizophrenic Patients

NAME	EXP.	SEX	AGE	EDUC*	SYMPTOMS**	DUR.	MEDIC.***	R-L 100
WW	1	M	21	11	WI, P, HV HA, IOC, HS	1 yr.	Hal	18
PL	1	M	20	?	WI, D, P, HA	1 mo.	Hal	79
JM	1	M	17	7	HV, D, HA IOC, P	4 yrs.	CPZ, DP, FLD, Flu	27
SB	1	M	19	12	HA, E, IOR, IOC, D, TI P, WI	6 mos.	Hal	29
LC	1, 3	M	23	12	HA, P, HS	2 yr.	Thi	120
DS	1, 3	M	20	13	AX, P, WI	4 yr.	Hal, Alp	35
RW	1, 3	M	21	12	P, D, IOR AB	1 mo.	Hal, Ben	8
JL	1, 3	F	46	12	HA, P, TD	20 yr.	Thi	90
AH	1, 3	M	34	10	AB, HA, P, HV, IOR, D	15 yr.	FLD, Ben	86
HD ⁺	1, 3	M	22	11	HA, P, TI, IOC, HO, IOR, D	1 yr.	Never medicated	149
FP ⁺	1, 3	M	20	11	AB, ASP D, P,	>6 mos.	Never medicated	6
SCHN	1, 3	M	16	10	D, WI	<6mos.	Never medicated	37
PD	3	F	26	12	HA, D, HV, IOR	12 yr.	Hal, KCl, Las	-
AM ⁺	3	F	29	20	P, HA, IOR	3 mos.	Never medicated	-
RS ¹⁺	3	M	31	23	D, P, IOR	2 mos.	Never medicated	-

⁺ Tested while neuroleptical naive and after medication (Fig. 9)

¹ This subject was not included in Exp. 3 (Fig. 8) but replaced DS (who died) in the pre-post study (Fig. 9)

* Highest grade level; 17-20 = college, 21-24 = graduate school

** (See next page for symptoms) *** (see next page for medications)

Table 1

Characteristics of Schizophrenia Patients (continued)

**

Ab = Substance abuse
 ASP = Antisocial Personality
 Ax = Anxiety
 D = Delusions
 E = Echolalia
 HA = Hallucinations (auditory)
 HO = Hallucinations (olfactory)
 HS = Hallucinations (somatic)
 IOC = Ideas of Control
 IOR = Ideas of Reference
 P = Paranoid
 TI = Thought Insertion
 WI = Withdrawn

Alp = alprazolam
 Ben = benztropine
 CPZ = chlorpromazine
 DP = diphenhydramine
 Fl = fluphenazine
 Hal = haloperidol
 KCl = potassium chloride
 Las = lasix
 Lox = loxapine
 Mes = mesoridazine
 FLD = fluphenazine decanoate
 Thi = thioridazine

This research was supported in part by ONR Contract N0014-86-K-0289 and by a grant from the John D. and Catherine T. MacArthur Foundation.

END

10-87

DTIC